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STABILITY OF ENKEPHALIN AND CETYL-PEG₂-ENKEPHALIN
IN RAT BRAIN HOMOGENATE

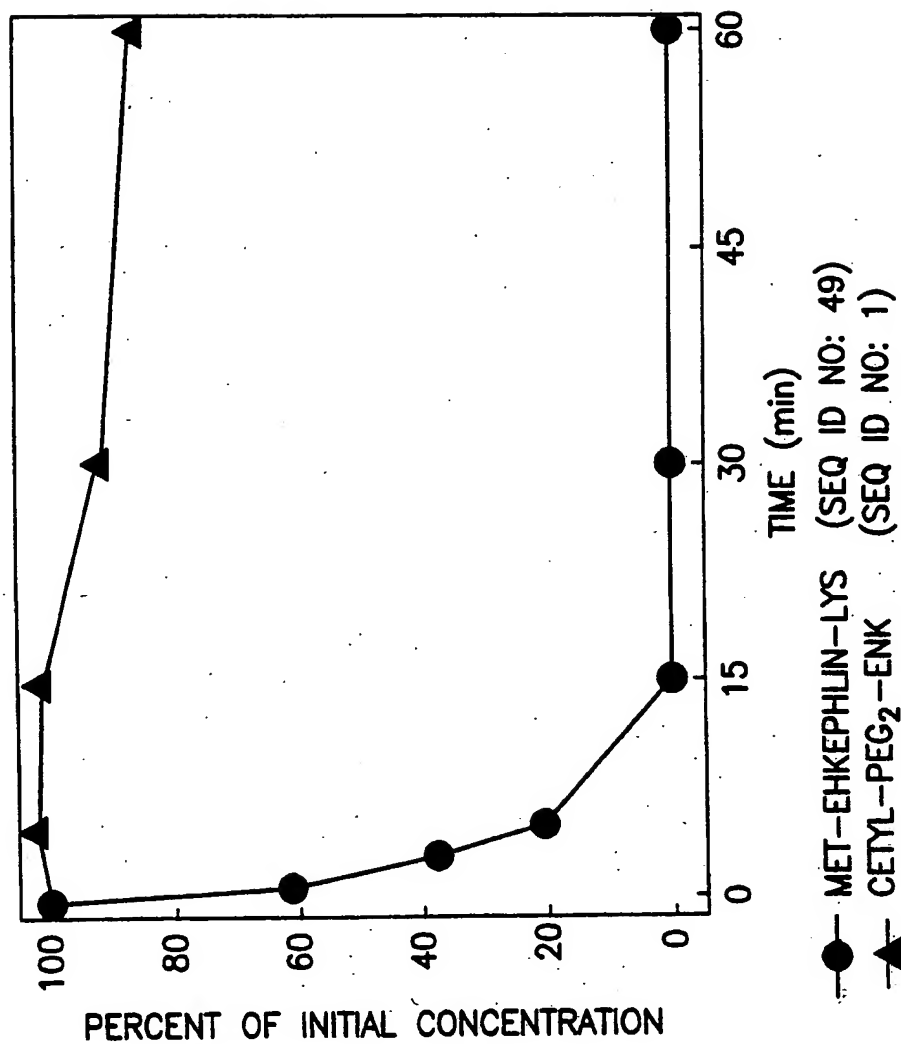


FIG.2

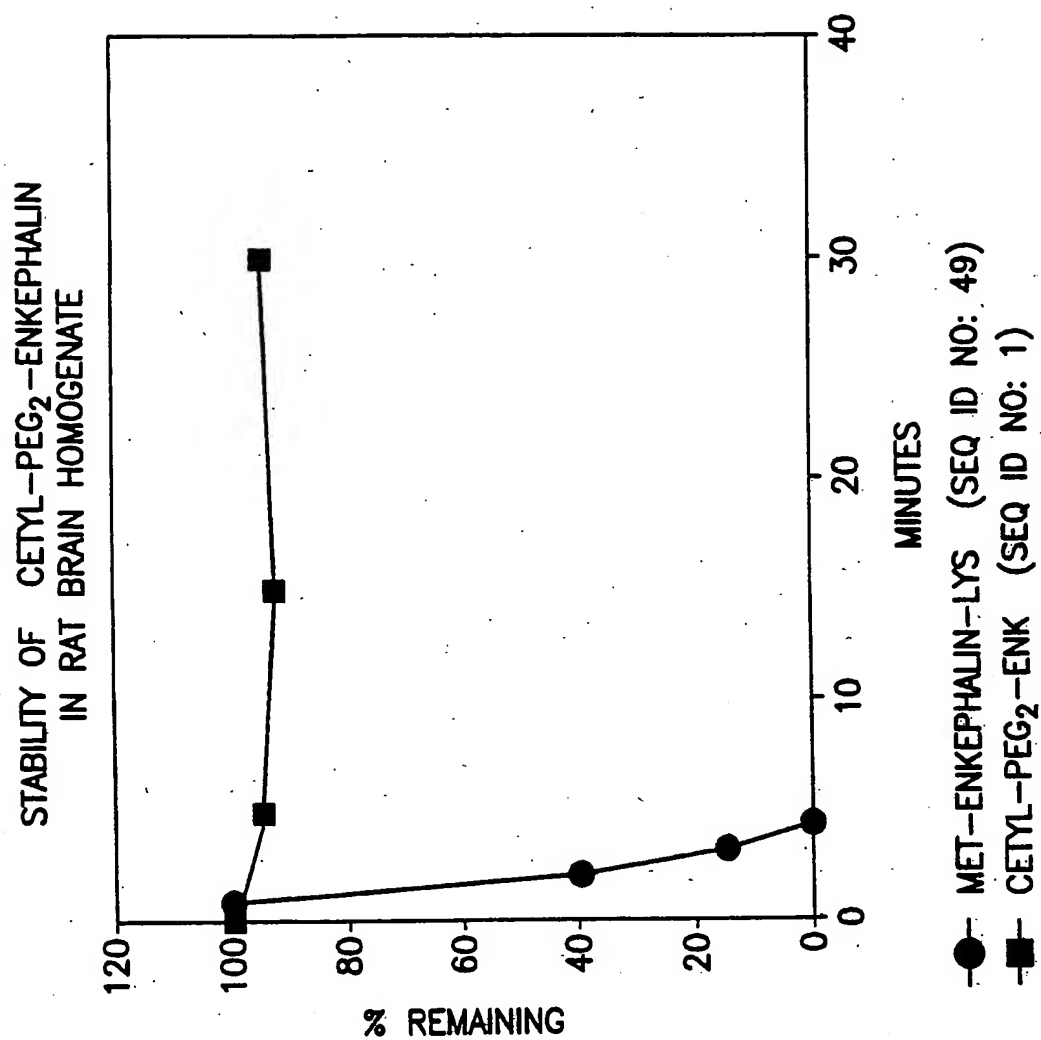


FIG.3

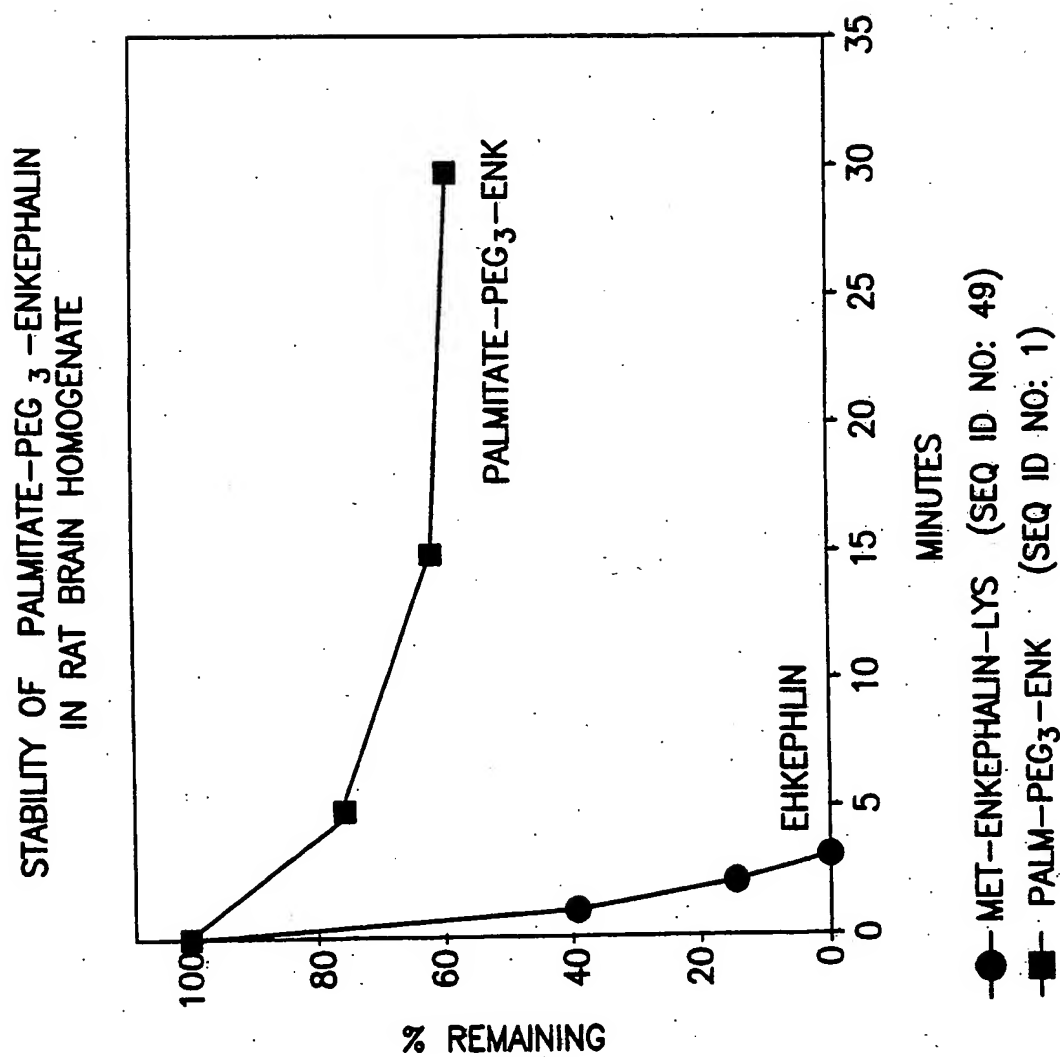


FIG.4

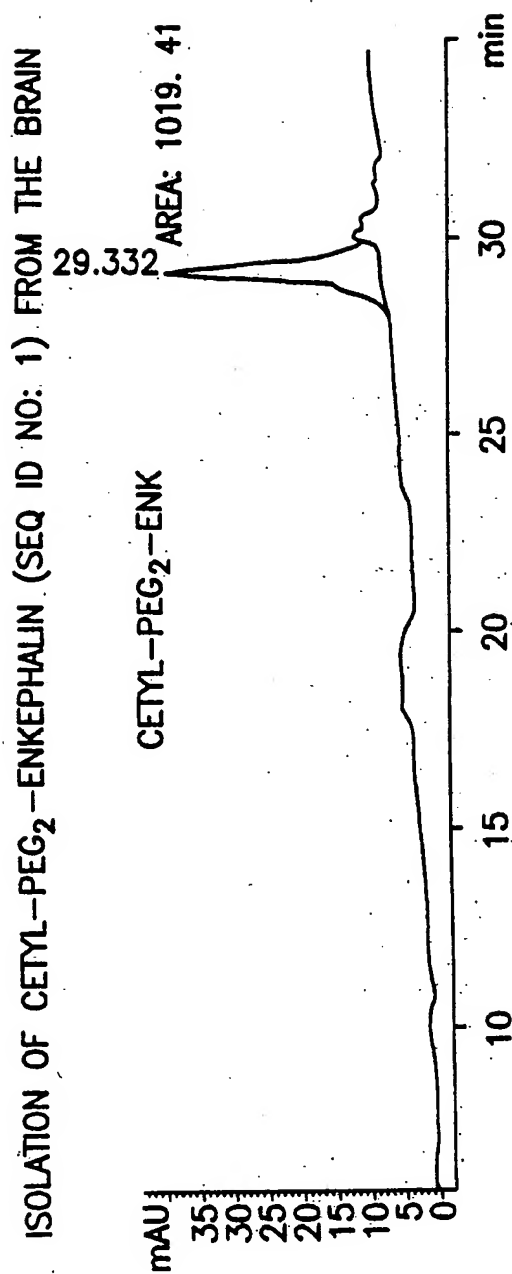


FIG. 5A

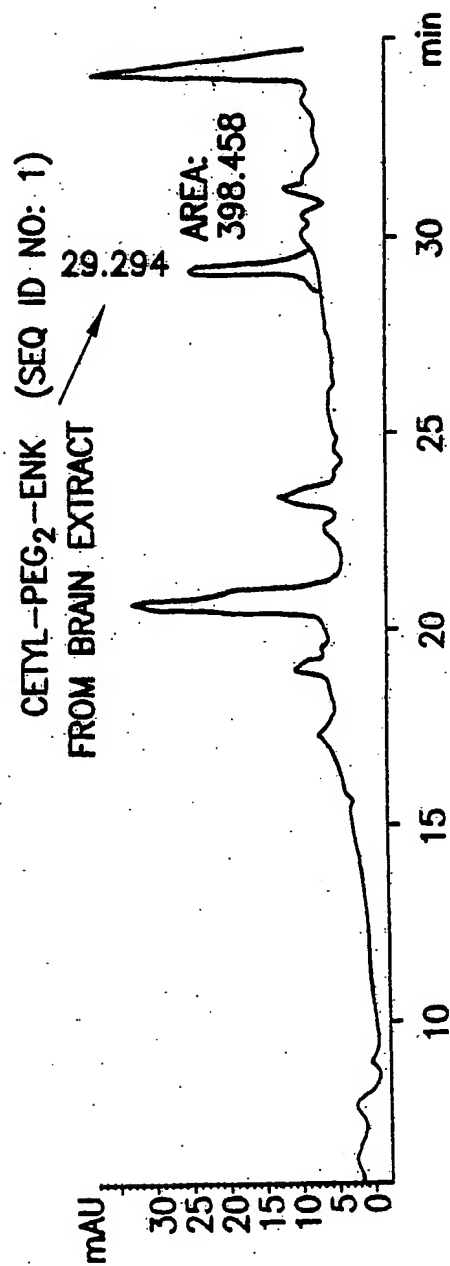


FIG. 5B

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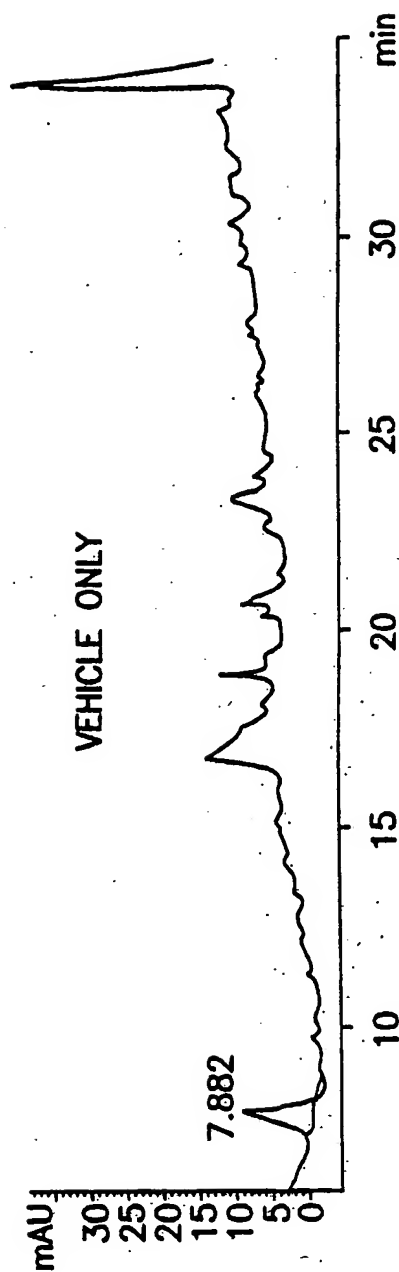


FIG.5C

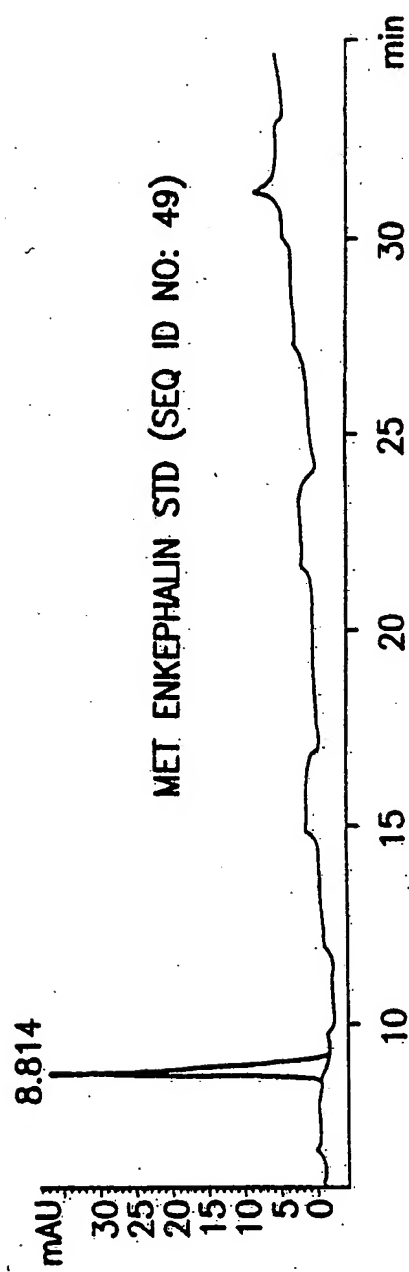


FIG.5D

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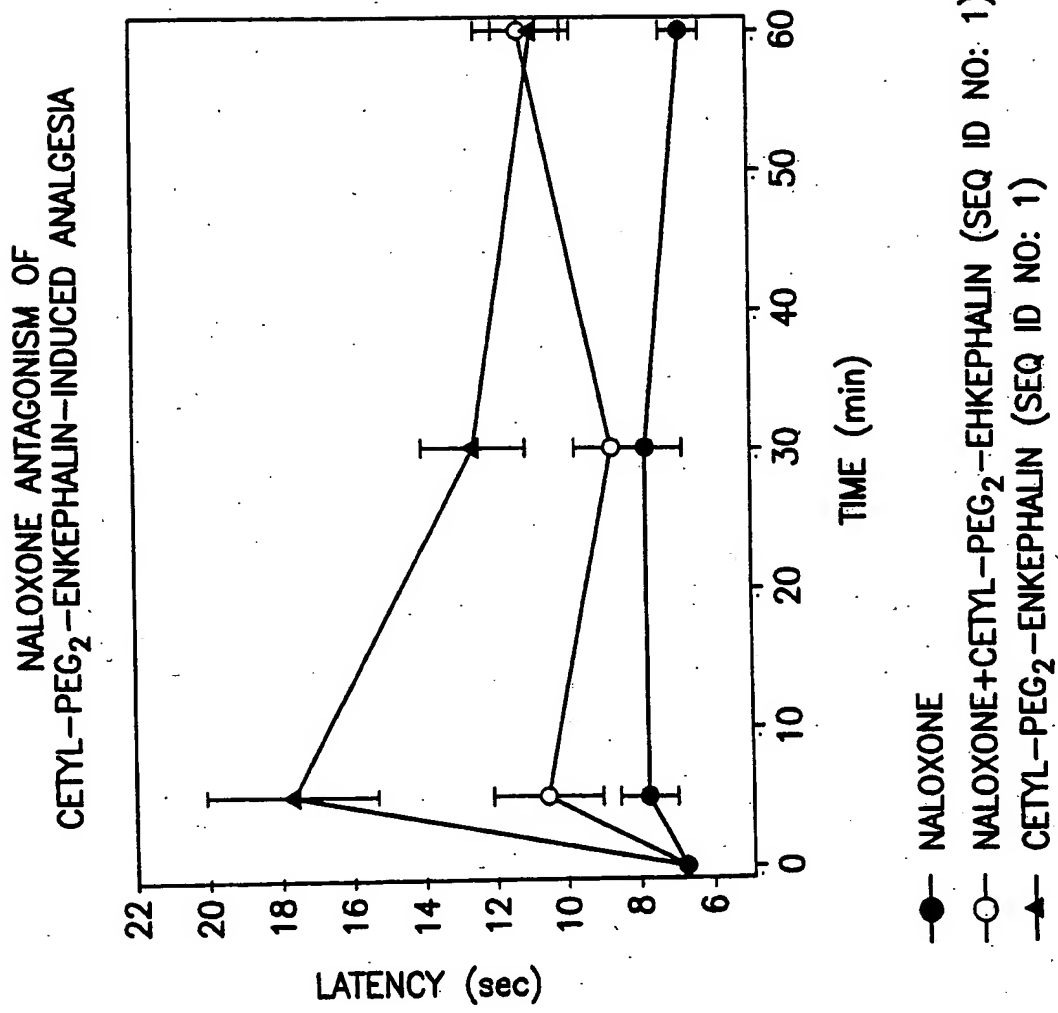


FIG.6

ANALGESIC EFFECT OF A 5 mg/kg IV DOSE OF CETYL-PEG₂-ENKEPHALIN (SEQ ID NO: 1)
MONOCONJUGATE IN THE RAT HOT-PLATE ASSAY

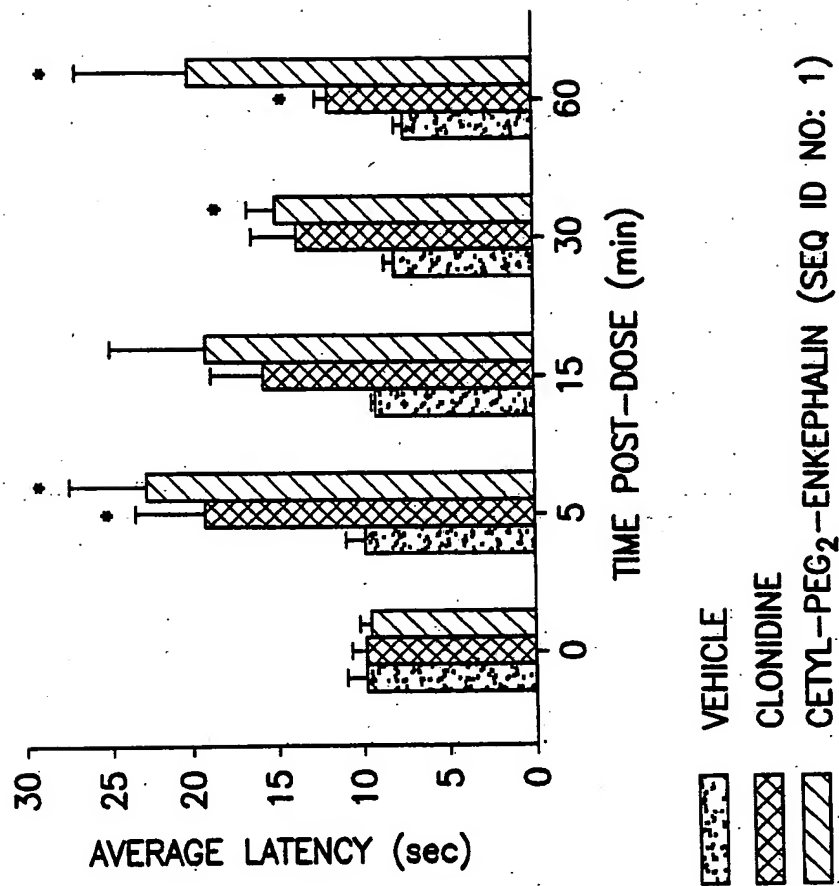
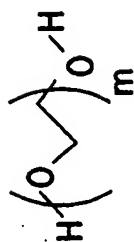


FIG.7

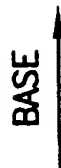
COMPARISON OF μ -RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES		
DRUG OR CONJUGATE	DETAILED STRUCTURE	% SPECIFIC BINDING
NALOXONE	NALOXONE	100
ENKEPHALIN	MET-ENKEPHALIN-LYS (SEQ ID NO: 49)	67
CETYL-ENK	CETYL-PEG ₂ -ENK (SEQ ID NO: 1)	100
CHOL-ENK	CHOLESTEROL-PEG ₃ -ENK (SEQ ID NO: 1)	95
DHA-ENK	DHA-PEG ₂ -ENK (SEQ ID NO: 1)	63
PALM-ENK	PALMITATE-PEG ₃ -ENK (SEQ ID NO: 1)	76
CETYL-TEG-ENK	CETYL-PEG ₃ -ENK (SEQ ID NO: 1)	100

FIG.8

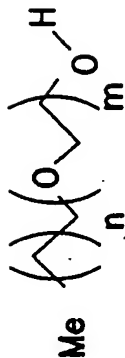
SYNTHESIS OF OLIGOMER



POLYETHYLENE GLYCOL
m=0, 1, 2, 3
(AVERAGE)



$\text{Me}-(\text{CH}_2)_n\text{Br}$
(BROMO ALKYL DERIVATIVE)
m=15, 17 etc.



AMPHIPHILIC POLYMER

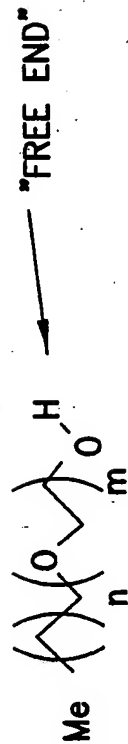
"FREE END"



AMPHIPHILIC POLYMER

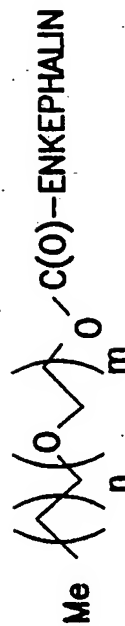
FIG.9

ATTACHMENT OF OLIGOMER TO ENKEPHALIN



ACTIVATION

ENKEPHALIN



OLIGOMER--ENKEPHALIN--CONJUGATE

EXAMPLE $m=14$ AND $n=2$ CETYL--PEG₂--ENKEPHALIN

FIG.10